

Applicants provide herewith evidence in support of a role of ZGGBP1 in bipolar affective disorder. See the attached Declaration of Dr. Flannery. The evidence shows that the occurrence of the single nucleotide polymorphism (SNP) in the ZGGBP1 gene is strongly correlated with bipolar affective disorder. The evidence provides clear support for the ideas recited in the specification that ZGGBP1 is associated with affective neurological disorders such as bipolar affective disorders (see, e.g., page 1, lines 3-6). Indeed, the title of the application "ZGGBP1, Novel Peptides Related to Bipolar Affective Disorder Type 1, Sequences and Uses Thereof" explicitly points out a role for ZGGBP1. Accordingly, the claimed subject matter has the specific and substantial utility of being useful for research, therapeutic, or diagnostic purposes, as well as in providing animal models of affective disorders, as disclosed in the specification on page 3, lines 22-31.

The role of ZGGBP1 in bipolar affective disorder is further strengthened by the fact that Applicants isolated the ZGGBP1 gene by using the "positional cloning" approach. As described in the specification (see, e.g., page 9, lines 12-30), ZGGBP1 was identified by positional cloning in a region of chromosome 18q21, to which the genetic disorder, bipolar affective disorder, was mapped. The overall strategy of positional cloning is to map the location of a human disease gene by linkage analysis and then to use the mapped location on the chromosome to clone the gene. Numerous disease genes have been successfully identified this way, for example, the disease genes for Huntington's disease, cystic fibrosis, breast cancer, and diabetes. This technique reinforces the association with bipolar affective disorder that suggested from its homology with the known mouse NEDD4 sequence, as taught in the specification. Therefore, one skilled in the art would readily understand that the ZGGBP1 gene is indeed correlated with bipolar affective disorder.

Taken together, Applicants have provided evidence supporting a role of ZGGBP1 at least in bipolar affective disorder, contrary to the Examiner's assertion that "there is no evidence of record, which associates the instant polypeptides with any disease or disorder, or any specific and credible biological activity." Accordingly, Applicants have satisfied the requirements under 35 U.S.C. § 101. For the same reasons, Applicants have also satisfied the requirements under 35 U.S.C. § 112, first paragraph. Reconsideration and withdrawal of the rejections are respectfully requested.

CONCLUSION

In view of the foregoing remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945**.

Respectfully Submitted,

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